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APPLICATION NUMBER	FILING DATE	FIRST NAMED APPLICANT	ATTORNEY DOCKET NO.
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BARBARA G MCCLUNG
CHIRON CORPORATION
INTELLECTUAL PROPERTY DEPARTMENT R440
P O BOX 8097
EMERYVILLE CA 94662-8097

EXAMINER	
WORTMAN, D	
ART UNIT	PAPER NUMBER
1815	41

DATE MAILED: 08/15/97

This is a communication from the examiner in charge of your application.
COMMISSIONER OF PATENTS AND TRADEMARKS

OFFICE ACTION SUMMARY

☒ Responsive to communication(s) filed on 5-19-97

☐ This action is **FINAL.**

☐ Since this application is in condition for allowance except for formal matters, **prosecution as to the merits is closed** in accordance with the practice under *Ex parte Quayle*, 1935 D.C. 11; 453 O.G. 213.

A shortened statutory period for response to this action is set to expire 3 month(s), or thirty days, whichever is longer, from the mailing date of this communication. Failure to respond within the period for response will cause the application to become abandoned. (35 U.S.C. § 133). Extensions of time may be obtained under the provisions of 37 CFR 1.136(a).

Disposition of Claims

☒ Claim(s) 1-9, 19, 36 is/are pending in the application.

Of the above, claim(s) _____ is/are withdrawn from consideration.

☐ Claim(s) _____ is/are allowed.

☒ Claim(s) 1-9, 19, 36 is/are rejected.

☐ Claim(s) _____ is/are objected to.

☐ Claims _____ are subject to restriction or election requirement.

Application Papers

☐ See the attached Notice of Draftsperson's Patent Drawing Review, PTO-948.

☐ The drawing(s) filed on _____ is/are objected to by the Examiner.

☐ The proposed drawing correction, filed on _____ is ☐ approved ☐ disapproved.

☐ The specification is objected to by the Examiner.

☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. § 119

☐ Acknowledgement is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d).

☐ All ☐ Some* ☐ None of the CERTIFIED copies of the priority documents have been

☐ received.

☐ received in Application No. (Series Code/Serial Number) _____.

☐ received in this national stage application from the International Bureau (PCT Rule 17.2(a)).

*Certified copies not received: _____.

☐ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. § 119(e).

Attachment(s)

☐ Notice of Reference Cited, PTO-892

☐ Information Disclosure Statement(s), PTO-1449, Paper No(s). _____

☐ Interview Summary, PTO-413

☐ Notice of Draftsperson's Patent Drawing Review, PTO-948

☐ Notice of Informal Patent Application, PTO-152

– SEE OFFICE ACTION ON THE FOLLOWING PAGES –

Claims 1-9, 29 and 36 remain pending and under examination at this time.

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless --
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 1, 5, 6 and 9 are rejected under 35 U.S.C. 102(b) as being anticipated by Idson ("Pharmaceutical Emulsions," in Pharmaceutical Dosage Forms, Vol. 1 (Lieberman et al., eds.) Marcel Dekker, New York, pp. 199-243, 1988) previously made of record on PTO 892 attached to Paper No. 38. Idson teaches parenteral nutrition preparations that are submicron compositions comprising 10-20% metabolizable oil (soybean, safflower or cottonseed oil) and .02-2.5% emulsifying agent (phospholipids or lecithin) and not including polyoxypropylene-polyoxyethylene block copolymer or muramyl peptides. See, e.g., page 222, third full paragraph, as well as Table 5, columns a, b, d, and e. The term "adjuvant" has not been given patentable weight because the recitation occurs in the preamble. A preamble is generally not accorded any patentable weight where it merely recites purpose or intended use, and where the body of the claim does not depend on the preamble for completeness. The instantly claimed subject matter is anticipated by the parenteral nutrition compositions of Idson because the term "adjuvant" has not been given patentable weight and because the open

language "comprising" does not preclude adding other materials such as glucose or glycerol, etc., which are also included in the parenteral nutrition preparations of Idson.

Claims 1, 5, 6 and 9 are rejected under 35 U.S.C. 102(b) as being anticipated by US Patent No. 4,647,586 to Mizushima et al., of record. This rejection which was previously withdrawn in error is being reapplied. Mizushima discloses pharmaceutical compositions that comprise an oil-in-water emulsions containing a metabolizable oil and a phospholipid emulsifier and do not include polyoxypropylene-polyoxyethylene block copolymer or muramyl peptides. Applicant's remarks in Paper No. 37 to the effect that Mizushima et al. do not disclose "An adjuvant composition" have been noted but not found persuasive because the term "adjuvant" has not been given patentable weight because the recitation occurs in the preamble. A preamble is generally not accorded any patentable weight where it merely recites purpose or intended use, and where the body of the claim does not depend on the preamble for completeness. The instantly claimed subject matter is anticipated by the pharmaceutical compositions of Mizushima et al. because the term "adjuvant" has not been given patentable weight and because the open language "comprising" does not preclude adding other materials such as the 4-biphenylylacetic acid ester which is also included by Mizushima et al.; consequently, the language of claims 1, 5, 6, and 9 does not distinguish over the pharmaceutical compositions disclosed by Mizushima et al.

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claims 1-9, 29 and 36 are rejected under 35 U.S.C. 103(a) as being unpatentable over Hoskinson et al. and Glass et al. in view of Idson and Remington for reasons of record in the previous Office action, Paper No. 38.

Applicant has argued that neither Glass nor Hoskinson teaches submicron oil-in-water adjuvant compositions but that both relate to the use of an emulsion with another agent, that Remington and Idson discuss known adjuvants and summarize physical properties of emulsions, and that the combination of references does not suggest that submicron oil-in-water emulsions can cause an adjuvant effect. Applicant has reviewed the individual teachings of each of the four references and asserted that the instant adjuvant does not require a second adjuvant as does the composition of Hoskinson, nor does the instant adjuvant serve as a depot for antigen release as does the composition of Glass. Applicant has referred to Ott et al. as showing experimental analysis of the mechanism of adjuvant activity for the present compositions; in particular, Ott discloses that 10% of labelled oil of "MF59" and 25% of the antigen was left at an injection site at 6 hours post-injection. Applicant further points to Ott as showing that an instant adjuvant and the antigen need

not be administered at the same site in order to be effective, and has submitted a Declaration under 37 CFR 1.132 that also demonstrates that the adjuvant "MF59" and the antigen need not be administered simultaneously nor at the same site.

These arguments and the Declaration have been considered but not found persuasive and sufficient, respectively, for the following reasons.

In response to applicant's argument that the references fail to show certain features of applicant's invention, it is noted that the features upon which applicant relies (i.e., that submicron oil-in-water emulsions alone can cause an adjuvant effect) are not recited in the rejected claims. Although the claims are interpreted in light of the specification, limitations from the specification are not read into the claims. *In re Van Guens*, 988 F.2d 1181, 26 USPQ2d 1057 (Fed. Cir. 1993). The language "comprising" does not preclude addition of any other component (including antigen) except for the specifically excluded polyoxypropylene-polyoxyethylene block copolymer or muramyl peptides. Further, as noted above, the recitation of "adjuvant" in the preamble has been given no patentable weight as discussed above. Thus claims 1-9, 29 and 36 are deemed obvious because as presently recited they do not distinguish over the compositions taught by the combination of references of record and because Applicant has not addressed the teachings of Idson and Remington that one would have been motivated to make microemulsions in order to obtain improved stability. With respect to the results reported in Ott et al. and those shown in the Declaration submitted as Paper No. 40, it is noted that no composition named "MF59"

could be found in the specification, and there is some uncertainty as to exactly what "MF59" and "MF59-0" mean. For example, at page 280, line 8, "MF59 (4.3% w/v squalene, 0.5% w/v Tween 80, 0.5% w/v Span 85)"; page 285, caption to Figure 6, "...MF59 containing 0.05, 0.11, 0.22, p.43, 0.86, or 1.72 mg squalene"; page 287, in the caption to Figure 8 (to which Applicant has referred in the previous response at the bottom of page 6), "Five groups of rabbits ... and 4.3 mg MF59-0 three times ..."). If Applicant wishes to rely on results obtained with "MF59" it will be necessary to qualify any mention of "MF59" with the exact formulation used in order that the record may be clear as to whether such results were in fact obtained with a composition that is encompassed by the claims. The Declaration at page 2, under "Materials and Methods," refers to the "MF59" used as "(a submicron oil-in-water adjuvant composition having 5% squalene (v/v), 0.5% polysorbitan 80, 0.5% sorbitan trioleate, in citrate buffer)," which composition falls within the limitations of the instant claims. However, neither the demonstration of adjuvant activity of a submicron composition when administered separately from the administration of the antigen, nor the demonstration of adjuvant activity when the composition is delivered to a site remote from the site of antigen delivery appears to be supported in the specification as an unexpected result (see MPEP 716.02(f)). Further, the demonstration of adjuvant activity for a single submicron composition is not commensurate in scope with the claims that encompass compositions with different oils and emulsifying agents in varying amounts (see MPEP 716.02(d)). Applicant's unsupported assertion that "certain oil-in-water emulsions having oil droplets substantially all of

which are less than 1 micron in diameter exhibit unexpectedly high adjuvant activity" is not persuasive in the absence of factual evidence that is commensurate in scope with the claims, since the only results shown are for a single oil-in-water emulsion.

Because this action contains grounds of rejection not presented in the previous Office action, it is made non-final. Any inconvenience is regretted.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Examiner Wortman whose telephone number is (703) 308-1032. The examiner can normally be reached on Monday through Thursday from 7:30 am to 5:00 pm. The examiner can also be reached on alternate Fridays.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Marian Knode, can be reached on (703) 308-4311. The fax phone number for this Group is (703) 305-3014.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the Group receptionist whose telephone number is (703) 308-0196.

Marian Knode

MARIAN C. KNODE
SUPERVISORY PATENT EXAMINER
GROUP 1800

Donna C. Wortman, Ph.D.
August 8, 1997